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Should sperm be cryopreserved after spinal cord injury?

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Abstract

In spinal cord injured (SCI) patients, three main factors may cause infertility: erectile dysfunction, ejaculatory dysfunction and impaired semen quality. This letter aims to discuss how we can manage SCI patients' fertility in accordance with patient-centred care. For such SCI patients aged 20 to 40, having children represents hope for the future. Furthermore, it is a way to rebuild a life after the spinal injury and must be seen as an important part of the rehabilitation program. We suggest that sperm cryopreservation may contribute to patient-centred care management of SCI patients' fertility, although there is no scientific evidence that cryopreservation will improve fertility outcome after SCI. Indeed, sperm cryopreservation is an affordable and simple technique in specialised centres with trained staff. Here, a protocol to manage SCI patients' fertility is discussed: we propose PVS for sperm banking to all SCI patients after the phase of spinal shock during the rehabilitation program. If live sperm are retrieved, they are frozen and stored; however, if no live sperm are retrieved, electroejaculation and/or surgical sperm extraction are proposed only for patients who desire biological fatherhood. Prospective studies on the evolution of semen parameters, ejaculatory dysfunction, post-infectious obstructions and spermatogenesis impairment in chronic SCI patients are urgently needed to provide robust data for the evidence-based management of SCI patients' fertility. Even if use rates are expected to be low, sperm banking may be a simple and affordable preventative measure for selected male SCI patients.

Keywords: Spinal cord injury, Fertility preservation, Sperm banking, Semen parameters, Spermatogenesis

Résumé

Chez les patients blessés médullaires (BM), trois facteurs principaux peuvent provoquer une infertilité : la dysfonction érectile, la dyséjaculation et l'altération des paramètres spermatiques. Cette lettre a pour but de discuter comment gérer la fertilité des BM en accord avec le principe de soins axés sur le patient. Pour ces patients principalement âgés de 20 à 40 ans, la paternité représente un espoir pour le futur et un moyen de se reconstruire après la lésion médullaire ; cet aspect doit être considéré comme une partie importante du programme de réhabilitation. Nous suggérons que la cryoconservation de sperme (CS) chez le BM pourrait contribuer au principe de soins axés sur le patient, bien qu'il n'y ait pas de preuve scientifique que la CS améliore les résultats en assistance médicale à la procréation. En effet, la CS est une technique abordable et simple dans les centres

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spécialisés au personnel entraîné. Un protocole de prise en charge de la fertilité du BM est discuté : nous proposons la stimulation vibratoire pénienne à tous les patients BM après la phase de choc spinal, au cours du séjour en rééducation fonctionnelle. Si des spermatozoïdes sont obtenus dans l'éjaculat, ils sont cryoconservés ; dans le cas contraire, nous proposons une électroéjaculation et/ou un prélèvement chirurgical de spermatozoïdes seulement aux patients présentant un désir parental actuel. Afin d'assurer une gestion de la fertilité des BM basée sur des preuves scientifiques solides, des études prospectives de l'évolution à long terme des paramètres spermatiques, de la capacité à éjaculer, des obstructions post-infectieuses du tractus séminal et des altérations de la spermatogenèse chez les patients BM chroniques sont urgemment nécessaires. Dans l'attente de ces données, même si les taux d'utilisation attendus des paillettes sont faibles, la CS pourrait être une mesure préventive simple et abordable pour les patients BM.

Mots-clés: Lésion médullaire, Préservation de la fertilité, Congélation de sperme, Paramètres spermatiques, Spermatogenèse

Letter to the editor

Introduction

Spinal cord injury (SCI) mainly affects young male patients, the majority of whom live for a long time with SCI and often wish to become fathers during their post-injury life [1]. Nevertheless, difficulties generally occur when they try to achieve fatherhood by biological means. Indeed, in SCI patients, three main factors may cause infertility: erectile dysfunction, ejaculatory dysfunction and impaired semen parameters [2,3]. According to two retrospective studies, semen parameters do not significantly decrease during the long-term evolution of SCI patients [1,4,5], which led the authors to conclude that fertility preservation by early sperm banking is not indicated in SCI patients. The long-term management of SCI patients' fertility is based on diverse medical practices. Kafetsoulis et al. showed that in 28% of fertility centres, surgical sperm extraction, rather than semen retrieval, was used as a first line of treatment for the medical condition of anejaculation [6]. The main reasons for this practice were a lack of equipment and/or a lack of training to use penile vibratory stimulation (PVS) and electroejaculation (EEJ) to obtain ejaculated sperm.

Surgical sperm retrieval in SCI patients, as a first line of treatment, is not the best fertility management approach for two reasons. First, SCI patients are affected by frequent co-morbidities; consequently, surgery should be strictly limited to patients exhibiting specific indications [7,8]. Second, surgical sperm extraction generates a smaller quantity of lower quality sperm than ejaculation, and it generally commits patients to more invasive assisted reproductive techniques (ART), such as intracytoplasmic sperm injection (ICSI), than ejaculated sperm, which often allows in vitro fertilisation (IVF) or intra-uterine insemination (IUI) [9]. These two reasons are important from a financial point of view (for many couples, the cost of ICSI is very high) and also from a patient-centred care perspective because fertility patients attach importance to patient centeredness, which is not optimal in this type of management [10].

The aim of this letter is to address how we can manage SCI patients' fertility in accordance with patient-centred care.

The way to biological fatherhood

When a chronic SCI patient starts infertility treatments and no sperm has been banked, ART using fresh sperm is usually proposed. The ability of the patient to retrieve ejaculated semen, the semen parameters and the feminine characteristics are analysed to choose the technique that would provide the best pregnancy chances for the couple: self-inseminations at home or IUI/IVF using sperm selected from ejaculated semen [6,11,12]. If masturbation, PVS with Midodrine adjunction, and EEJ cannot result in ejaculation, sperm is surgically retrieved from the seminal tract/testis [11-13]. Surgical sperm extraction is also used when azoospermia is diagnosed in the ejaculate or in cases of severely impaired motility and viability. Indeed, it has been demonstrated that, in SCI patients, sperm motility is better in the Vas deferens than in the ejaculate [14].

Sperm cryopreservation may contribute to the patient-centred care management of SCI patients' fertility

From the SCI patient's perspective, sperm cryopreservation may help address three concerns: 1) anxiety about future fertility, 2) higher risk of infertility during the chronic phase, and 3) the type of fertility management when pursuing biological parenthood.

1) For most SCI patients aged 20 to 40, having children represents hope for the future and is a way to rebuild a life after the spinal injury; thus, it must be seen as an important part of the rehabilitation program. In some patients, preventative sperm cryopreservation may help relieve

anxiety about their future fertility [15,16]. Sperm banking may also decrease anxiety on the day of ART; indeed, in most SCI patients, sperm recovery presents more challenges than in neurologically intact men, most of whom can retrieve their semen by masturbation. Most infertility centers therefore prefer to use banked sperm on the day of ART.

2) In chronic SCI patients, the evolution of fertility is at higher risk than in non-SCI infertile patients. Indeed, four factors are more frequent in SCI than in infertile patients: semen parameters impairment, oxidative stress, genital tract infections, and ejaculatory dysfunction.

A prospective study is the most appropriate study design for assessing the long-time evolution of semen parameters in SCI patients; to our knowledge, no prospective studies have been performed to address this issue. Retrospective studies have shown that more than 90% of SCI patients display impaired semen parameters characterised by asthenospermia, necrospermia, leukocytospermia but normal or reduced ejaculate volume and normal sperm concentration [1-5,17]. Nevertheless, it is known that conventional semen parameter analyses provide insufficient information for the evaluation of male fertility potential and in distinguishing between infertile and fertile men [18]. Indeed, sperm deficiencies that critically affect pregnancy rates, such as DNA fragmentation, oxidative damage and antisperm antibodies, can only be assessed by sperm functional tests [19]. ROS decrease the ability of spermatozoa to fertilise the oocyte by damaging the sperm membrane, which impairs its motility, and by damaging sperm DNA, which impairs its genomic contribution to the zygote [20]. Defective sperm chromatin structure, including DNA fragmentation, is negatively associated with fertility [21]. To our knowledge, the long-term stability of sperm DNA fragmentation and ROS levels in SCI patients has not been established. Increased oxidative stress could impair testicular microvascularisation and hormonal environment [22]. In this case, a patient's chances of pregnancy could be impaired by using fresh semen with less favourable characteristics than previously banked frozen-thawed semen.

Infections of the accessory sex glands are observed in 10% of non-SCI infertile patients [23] and in 28-38% of SCI patients [24,25]. Very few reports have examined the effective consequences of such infections when compared to their high frequency in this population. Patients with an accessory gland infection show higher oxidative stress in their semen, and chronic infections could impair the epithelium function of accessory glands, leading to decreased sperm viability and motility [23,26]. Moreover, acute infections, such as orchitis and epididymitis, are associated with a higher risk of seminal tract obstruction [20,26,27]. In cases of obstructive azoospermia, sperm can only be retrieved by surgery, and the patient's chances of pregnancy could be lower than without obstruction.

Although there are no data showing the development of an impairment over time relative to SCI patients' ability to ejaculate, a recent study suggested that intradetrusor injections of botulinum toxin could induce retrograde ejaculation and reduce ejaculate volume by spreading to the bladder neck [28]. This treatment of overactive bladders and bladder sphincter dyssynergia has had a remarkable effect in patients with SCI and is increasingly used in this population [29].

Moreover, the individual abilities of SCI patients to achieve ejaculation have not been shown to be stable during the chronic phase: consequently, EEJ or surgical sperm extraction could become necessary in some chronic SCI patients who were originally able to ejaculate.

3) When chronic SCI patients start infertility treatments, more than one fertility centre out of four lacks equipment and/or training to obtain ejaculation by PVS and/or EEJ [6] which limits patients to surgical sperm extraction only. As sperm banking is a more complex procedure in SCI patients than in neurologically intact patients, performing this procedure while the patient is still in the rehabilitation centre with trained physicians and biologists could be beneficial.

There is no scientific proof that cryopreservation will improve fertility outcomes after SCI

For SCI patients, sperm banking could be argued to be inappropriate because the use of frozen sperm does not significantly improve the results of ART compared to the results obtained with fresh sperm. Deforge et al. stated that "unless carried out in the first 1 or 2 weeks after SCI, there is no utility in freezing the sperm" [30], because sperm motility is impaired after freezing-thawing. Ferreira et al. demonstrated that in SCI patients, cryopreservation induces a decrease in sperm motility and mitochondrial activity and an increase in DNA fragmentation [17]. Nevertheless, these alterations were not more serious in sperm from SCI patients than in sperm from non-SCI patients, confirming the findings of Padron et al. [31]. Most studies showed that ART management of SCI patients without systematic sperm banking leads to a mean live birth rate of 40% [30], which is comparable to the rates for non-SCI patients. These similarities were observed in studies using IUI, IVF and ICSI [6]. Other studies showed a lower success rate in couples with SCI male partners than in couples with another male factor of infertility [32].

Sperm cryopreservation is affordable and simple in specialised centres

Our approach for fertility management is to propose sperm banking to all SCI patients. We suggest performing

this procedure after the phase of spinal shock while the patient is still in the rehabilitation centre so that he may benefit from the specialised equipment and trained staff. If live sperm are retrieved, they should be frozen and stored [33]; however, if no live sperm are retrieved, EEJ and/or surgical sperm extraction should be proposed only to patients whose future goals include biological fatherhood.

Indeed, when no ejaculation can be obtained for ART treatment, from the patient-centred care and financial points of view, it is preferable to use banked sperm rather than to perform surgical sperm extractions.

Sperm banking should be proposed to SCI patients even if the use rate of banked sperm is expected to be low. Similarly, oncologists propose sperm banking to all young cancer patients before chemotherapy, although it has been shown that more than 70% of cancer patients recover spermatogenesis after cancer treatment and that the use rate of banked sperm is very low (6%) [34-36].

Conclusions

Prospective studies on the evolution of semen parameters, ejaculatory dysfunction, post-infectious obstructions and spermatogenesis impairments in chronic SCI patients are urgently needed to provide robust data for an evidence-based management approach to SCI patients' fertility.

Until such an approach is established, sperm banking in rehabilitation centres remains a simple, safe and affordable preventative procedure for fertility management. Because SCI patients' fertility is at risk, we propose that fertility preservation should be considered for all of these individuals. Although the use rates are expected to be low, selected patients with SCI may benefit from this procedure: sperm banking could improve the patient-centred care and cost of fertility treatment by decreasing the rate of surgical sperm extraction and ICSI.

Abbreviations

ART: Assisted reproduction technique; EEJ: Electro-ejaculation; ICSI: Intracytoplasmic sperm injection; IUI: Intra-uterine insemination; IVF: In vitro fertilisation; PVS: Penile vibratory stimulation; ROS: Reactive oxygen species; SCI: Spinal cord injury.

Competing interests

None of the authors declare any conflict of interest.

Authors' contributions

JP, GK, and BB performed literature search and compiled the bibliography. GK, JMR and JP conceived the discussion. GK and JP drafted the manuscript. BB, CMG, JMG and JSM revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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